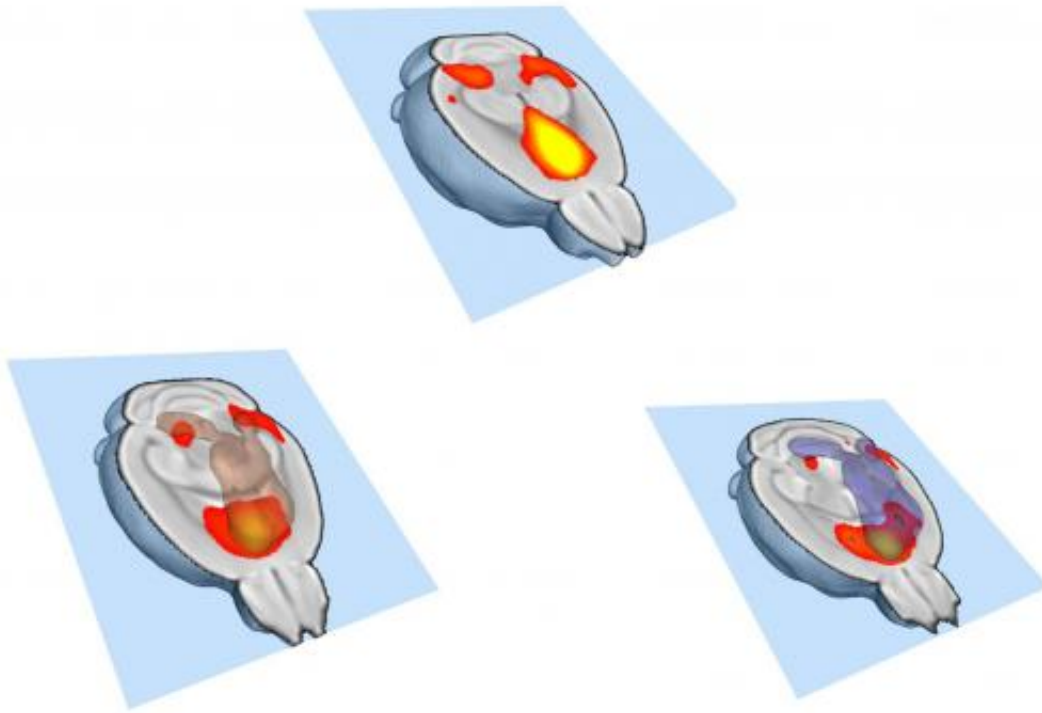


Making your brain social: Failure to eliminate links between neurons produces autistic-like mice

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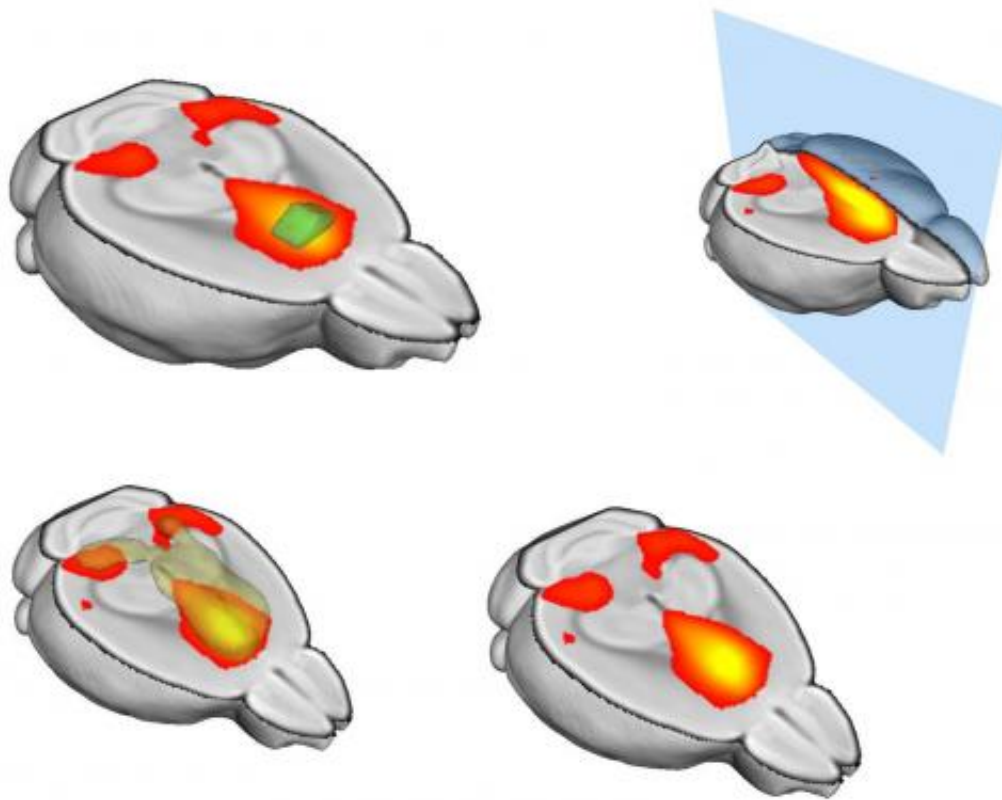
A series of mouse brain schemes showing in heat map the functional connectivity between a defined pre-frontal cortex (PFC) regions and other areas of the brain in wild-type mice as measured by resting-state functional MRI. The blue 3D shape in some images indicates the volume of thresholded significant functional connectivity with PFC. This connectivity is significantly reduced in mice with deficient neuron-microglia signalling and this deficit in connectivity resembles that seen in autistic persons. Credit: Adam Liska, Alessandro Gozzi, IIT

In many people with autism and other neurodevelopmental disorders, different parts of the brain don't talk to each other very well. Scientists have now identified, for the first time, a way in which this decreased functional connectivity can come about. In a study published online today in *Nature Neuroscience*, scientists at the European Molecular Biology Laboratory (EMBL) in Monterotondo, Italy, and collaborators at the Istituto Italiano di Tecnologia (IIT), in Rovereto, and La Sapienza University in Rome, demonstrate that it can be caused by cells called microglia failing to trim connections between neurons.

"We show that a deficit in microglia during development can have widespread and long-lasting effects on brain wiring and behaviour," says Cornelius Gross, who led the study. "It leads to weak brain connectivity, decreased [social behaviour](#), and increased [repetitive behaviour](#), all hallmarks of autism."

The findings indicate that, by trimming surplus connections in the developing brain, microglia allow the remaining links to grow stronger, like high-speed fibre-optic cables carrying strong signals between [brain regions](#). But if these cells fail to do their job at that crucial stage of development, those brain regions are left with a weaker communication network, which in turn has lifelong effects on behaviour.

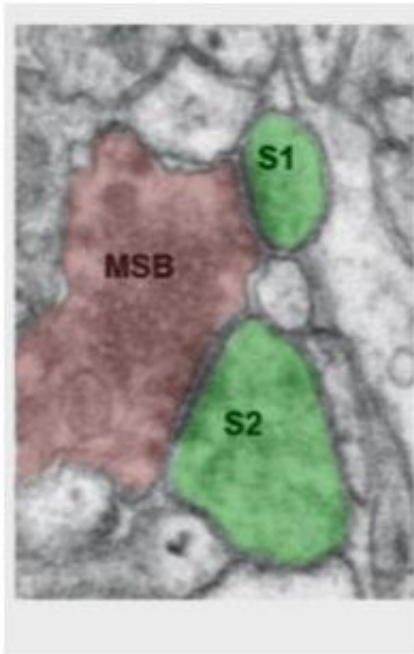
Yang Zhan, a postdoctoral fellow in Gross' lab at EMBL, analysed the strength of connections between different areas of brain in [mice](#) that were genetically engineered to have fewer microglia during development. Working with Alessandro Gozzi's lab at IIT and Davide Ragozzino at La Sapienza University, the EMBL scientists combined this approach with high-resolution fMRI (functional Magnetic Resonance Imaging) scans of the mice's brains, taking full advantage of a novel technique developed at IIT, which enables scientists to obtain detailed, three-dimensional maps of the brain's functional connections.



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The team found that mice with fewer microglia had weaker connections between neurons, and less cross-talk between different brain regions. When Rosa Paolicelli, a PhD student in Gross' lab, studied the mice's behaviour, she discovered that mice with fewer microglia and decreased connectivity displayed behaviours commonly associated with [autism](#)

[spectrum disorders](#). These mice spent more time repeatedly grooming themselves, and avoided social interactions.



An electron microscope image from the hippocampus of a wild-type mouse pre-synaptic bouton in which you can clearly see neurotransmitter vesicles making synapses with two spines from another neuron. The presence of this form of “double” synapse, called multi-synapse bouton (MSB), typically increases dramatically as the brain matures during the early postnatal period and is absent in mice with deficient neuron-microglia signalling, presumably due to their failure to prune unwanted synapses and allow for the surviving synapses to strengthen, or “double”, their synaptic contacts. Credit: Giulia Bolasco, EMBL

"This is an exciting time to be studying microglia," Gross concludes: "they're turning out to be major players in how our brain gets wired up."

Provided by European Molecular Biology Laboratory

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